

Attorney's Docket No.: JYG122USA

TRANSMITTAL LETTER TO THE U.S. ELECTED OFFICE
(EO/US) - ENTRY INTO NATIONAL STAGE UNDER 35 USC 371PCT/GB98/03137

International Application No.

21 October 1998

International Filing Date

23 October 1997

Priority Date Claimed

METHODS OF CONTROLLING HOUSE DUST MITES AND BEDMITES

Title of Invention

Roland Cox
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Applicant(s), Residence Addresses and Citizenship for EO/US

Box PCT
Assistant Commissioner for Patents
Washington, DC 20231
Attn. EO/US

Sir:

Applicant herewith submits to the United States Elected Office (EO/US) the following items under 35 USC 371:

- (1) This express request to immediately begin national examination procedures (35 USC 371(f)).
- (2) A copy of the international application: one cover page, seven pages of specification, two pages of claims, and two pages of International Search Report.
- (3) A five page executed Declaration and Power of Attorney.
- (4) A copy of the three page Request form.
- (5) A First Preliminary Amendment which cancels the multiple dependent claim and which should be entered before the calculation of the filing fee.
- (6) Our check in the amount of \$996 covering the basic national fee as set forth in 37 CFR 1.492(a)(5). (17 claims in total; 5 independent; and no multiple dependent).
- (7) A Second Preliminary Amendment.

09/529690
422 Rec'd PCT/PTO 18 APR 2000

Copies of the following miscellaneous items are also enclosed:

- (8) Copy of the three page Demand for International Preliminary Examination.
- (9) Copy of the six page International Preliminary Examination Report, dated August 12, 1999.
- (10) Copy of the one page Notification of the Recording of Name Change, Form PCT/IB/306, "Akzo Nobel UK plc" to "Akzo Nobel UK Limited".

Please charge any additional fees which may be required to effect entry into the National Phase and credit any overpayment to our deposit account 08-3040.

Please direct all communications concerning this application to the undersigned.

Respectfully submitted,
Howson and Howson
Attorneys for the Applicant

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GPO: 2000 OMB NO. 1110-0002

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JYG122USA

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:)
Roland Cox) Examiner:
Application No.:) Group Art Unit:
Corresponding International Filing No.:)
PCT/GB98/03137)
Filed: Herewith)
For: METHODS OF CONTROLLING)
HOUSE DUST MITES AND)
BEDMITES) April 18, 2000

Box PCT
Assistant Commissioner for Patents
Washington, DC 20231

FIRST PRELIMINARY AMENDMENT

Sir:

Before calculating the filing fee, please amend the above-identified patent application as follows.

In the Claims

Cancel claims 5 and 9.

REMARKS

Please enter this preliminary amendment before calculating the filing fee. The multiple dependent claim has been canceled.

Charge any additional fees due to our deposit account no. 08-3040.

Respectfully submitted,
Howson and Howson
Attorneys for Applicant

By William Bak
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JYG122USA

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:)
Roland Cox) Examiner:
Application No.:) Group Art Unit:
Corresponding International Filing No.:)
PCT/GB98/03137)
Filed: Herewith)
For: METHODS OF CONTROLLING)
HOUSE DUST MITES AND)
BEDMITES) April 18, 2000

Box PCT
Assistant Commissioner for Patents
Washington, DC 20231

SECOND PRELIMINARY AMENDMENT

Sir:

Please amend the above-identified patent application as follows.

In the Abstract

Please enter the abstract on a separate page as attached.

In the Claims

Amend claims 6, 8 and 10, as follows.

In claim 6, line 1, replace "5" with --11--.

8 (Amended). A filling material for an article of bedding or an upholstered article, [characterised in that in said filling material is incorporated] comprising a compound which is incorporated in said filling material and which exhibits antifungal activity against fungi of at least one of the groups *Aspergillus glaucus* [and/or] and *A. restrictus*.

10 (Amended). A bedding fabric, [characterised in that it comprises] comprising a fibre having incorporated therein a chemical compound which has antifungal activity against fungi of at least one of the groups *Aspergillus glaucus* [and/or] and *A. restrictus*.

Add new claims 11-19, as follows.

11. The use according to claim 2, wherein the fibre is incorporated in a textile article.

12. A bedding or upholstered article, comprising a filling material having a compound which is incorporated therein and which exhibits antifungal activity against fungi of at least one of the groups *Aspergillus glaucus* and *A. restrictus*.

13. A method for controlling house dust mites and bedmites, comprising the step of using a polymeric article having incorporated therein a chemical compound which has antifungal activity against fungi of at least one of the groups *Aspergillus glaucus* and *A. restrictus*.

14. A method according to claim 13, wherein said polymeric article is a fibre.

15. A method according to claim 14, wherein said fibre is a manmade fibre into which said chemical compound was incorporated during manufacture of said manmade fibre.

16. A method according to claim 15, wherein said manmade fibre is an acrylic fibre.

17. A method according to claim 14, wherein said fibre is incorporated into a textile article.

18. A method according to claim 17, wherein said textile article is a bedding fabric.

19. A method according to claim 13, wherein said polymeric article is a foam.

REMARKS

Please enter this preliminary amendment after calculating the filing fee.

The attached abstract is substantially identical to the abstract published on the cover page of the published International application. The abstract is being added to conform with proper U.S. practice. No new matter was added.

Claims 5 and 9 were canceled in the First Preliminary Amendment. Claims 6, 8 and 10 have been amended and claims 11-19 have been added in this Preliminary Amendment. Thus, claims 1-4, 6-8 and 10-19 are presented for prosecution.

Canceled claim 5 has been rewritten as new claim 11, and canceled claim 9 has been rewritten as new claim 12. The subject matter in "use" claims 1-4, 6, 7 and 11 have been presented in new claims 13-19 as "method" claims. No new matter was added. The claim

amendments are believed to place the claims in better conformance with United States practice.

Thus, claims 1-4, 6, 7 and 11 begin with the preamble "The use" as printed in the corresponding International PCT application. Claims 13-19 are method claims which correspond to the limitations in the "use" claims 1-4, 6, 7 and 11. Claim 8 covers a filling material for a bedding or upholstery article, claim 12 covers a bedding or upholstery article having a filling material, and claim 10 covers a bedding fabric.

Applicant respectfully requests consideration of claims 1-4, 6-8 and 10-19.

Charge any additional fees due to our deposit account no. 08-3040.

Respectfully submitted,
Howson and Howson
Attorneys for Applicant

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METHODS OF CONTROLLING HOUSE DUST MITES AND BEDMITESField of the invention

This invention relates to methods of controlling house dust mites and bedmites (hereinafter HDM). HDM are typically 5 Dermatophagoides spp., one species of particular significance being D. pteronyssinus.

A major food source for HDM is dead skin fragments (dander). Such fragments are continually shed by humans in considerable quantities. HDM proliferate in particular in 10 bedding, including the fillings of pillows and mattresses, and in upholstered articles and fibrous floor coverings. HDM are xerophilic organisms which do not require liquid water, and they live in the absence thereof. They demand a high humidity environment, requiring a relative humidity (R.H.) 15 of about 70 to 80 percent to survive. They absorb little water from the atmosphere and are effectively reliant on their food as the source of water. HDM typically excrete about 20 dung pellets per day. These pellets are very dry and brittle and are about 30 micron in size. They are 20 readily broken up into particles about 1-10 micron in size. In the absence of free moisture, these particles readily acquire a positive static charge and become airborne. They are of respirable size and are accordingly able to enter the bronchial tubes of the human lung, where they become 25 deposited on the mucus layer in the tubes and absorb water. The particles contain toxins, which are released when the particle is hydrated, and they can cause rapid allergic reactions, including bronchial inflammation and asthmatic symptoms. One such allergenic toxin of major importance is 30 Der p I, which is a highly-stable water-soluble glycopeptide of molecular weight 30,000 derived from the digestive system of D. pteronyssinus.

Considerable effort has been expended in devising methods for controlling allergic reactions caused by the 35 presence of HDM. One general method is the topical use of

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acaricides (the generic name for substances lethal to mites). Other methods rely upon control of the allergenic particles, for example by encasing them or by denaturing or destroying the allergens they contain. A further method 5 relies on the topical application of fungicides. Dead skin fragments as shed have a very low moisture content and a high fat content. As such, they are a poor food source for HDM. Furthermore, HDM require a source of B-group vitamins. Certain microscopic fungi which thrive in the 10 absence of liquid water (xerophilic fungi) grow on dead skin fragments, and they have the ability to absorb moisture from the atmosphere. In consequence, the moisture content of the fragments is raised; their fat content is reduced; and furthermore B-group vitamins and ergosterol, a precursor of 15 vitamin D, are generated. All this makes the fragments a more suitable food source for HDM. Many such fungi belong to the Aspergillus glaucus and A. restrictus groups. Particular species include A. penicilloides and Eurotium repens (A. repens).

20 It is believed that Aspergillus spp. such as A. repens and A. penicilloides are not responsible per se for allergic reactions in humans of the kind induced by HDM.

Topical application of fungicides has the disadvantage that repeated treatment at regular intervals is required for 25 continued control of HDM. Furthermore, fungicides are inherently toxic materials, and domestic topical application of such substances has been criticised for that reason. It is an object of the invention to provide a means of overcoming these disadvantages.

30 Disclosure of the invention

According to the invention, there is provided in a first aspect the use of a polymeric article having incorporated therein a chemical compound which has antifungal activity against fungi of the groups Aspergillus 35 glaucus and/or A. restrictus as a means of controlling HDM.

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Particular species of such fungi include A. penicilloides and A. repens. A particular species of HDM is D. pteronyssinus. The chemical compound may exhibit fungicidal and/or fungistatic activity.

5 The polymeric article may be a natural article, for example a cellulosic fibre, into which the chemical compound has been incorporated by, for example, a dyeing process. Alternatively, which may be preferred, the polymeric article may be a manmade article such as a fibre or foam into which 10 the chemical compound has been incorporated by a dyeing process or, more preferably, during the course of its manufacture. In the case of a fibre, such a manmade article may be of a natural polymer such as cellulose or of a synthetic polymer such as an acrylic polymer based on 15 polyacrylonitrile. Manmade fibres are described, for example, in a series of articles entitled "Fibers" in Ullmann's Encyclopaedia of Industrial Chemistry, 5th edition (VCH Publishing), Vol. A10 (1987) and A11 (1988). In the case of a foam, the manmade article may be of a synthetic 20 polymer such as a polyurethane. Fibres are used for the manufacture of textile articles such as bedding fabrics (including sheets, blankets, pillowcases, mattress covers and the like), upholstery fabrics and floor coverings (carpets). Both fibres and foams are used as filling 25 materials in articles such as pillows, mattresses, duvets and cushions, in which dander may accumulate and HDM thrive. Foams are used as backing materials and underlays for carpets.

According to the invention there is provided in a 30 second aspect a filling material for an article of bedding or an upholstered article, characterised in that in said filling material is incorporated a chemical compound which exhibits antifungal activity against fungi of the groups Aspergillus glaucus and/or A. restrictus. The filling 35 material is preferably in fibrous form. The invention further provides an article of bedding or an upholstered article filled with such material. The invention further

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provides a carpeting material which includes a fibre or foam incorporating such a chemical compound.

Insects such as HDM and mammals such as humans on the one hand and fungi such as Aspergillus spp. on the other hand belong to different taxonomic kingdoms. Many substances are known which are toxic to organisms within one kingdom but are effectively non-toxic to organisms within other kingdoms. The same is true, although to increasingly lesser degrees, between the lower taxonomic divisions beginning with phyla, classes and orders. It is an advantage of the invention that it can make use of antifungal compounds having low toxicity to higher mammals including humans and domestic animals and to other domestic pet creatures. The use of such compounds is accordingly preferred.

Acrylic fibres which incorporate neutral organic fungicidal compounds such as tolnaftate (which is a preferred compound), bifonazole, clotrimazole, miconazole, dichlorophene or hexachlorophene are disclosed in GB-A-2,309,461, and these fibres may be preferred in the invention. Another suitable compound is triclosan. The amount of the fungicidal compound in such fibres is preferably in the range from 0.01 to 2 percent by weight on the weight of fibre. Similar amounts of such fungicidal compounds are suitable also in other kinds of polymeric article of the invention.

Incorporation of the antifungal compound within the polymeric article has the advantages that release of the compound into the environment is minimised and that the antifungal effect is long-lasting and endures throughout laundering and dry-cleaning. Wet-spun acrylic fibres may have the advantage of a fissured structure, which both confers good moisture transport properties and assists diffusion of the antifungal compound to the fibre surface following depletion therefrom. The low moisture regain of synthetic fibres such as acrylic fibres may also be

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advantageous in maintaining a low humidity environment and thereby interfering with growth of Aspergillus spp. and HDM.

The invention is illustrated by the following Example, in which parts and proportions are by weight unless otherwise specified:-

Example

This Example illustrates the fungicidal activity against A. repens of acrylic fibres which incorporate a fungicide and of the use of such fibres in controlling HDM.

10 Acrylic fibres containing 0.4% tolnaftate were prepared by a similar method to that disclosed in Example 1 of GB-A-2,309,461. Such fibres are available commercially from Courtaulds Fibres (Holdings) Limited under the Trade Mark AMICOR AF. Acrylic fibres containing no antifungal agent 15 (available from Courtaulds Fibres (Holdings) Limited under the Trade Mark COURTELLE) were used as control. The antimicrobial activity of the fibres was measured by the parallel streak method disclosed in Example 1 of GB-A-2,309,461, but using a culture of A. repens (IMI 20 094150) containing ca. 3×10^6 spores/ml. Test plates were incubated at 25°C for 4 days. The widths of inhibition zones of fungal growth were measured, and the results (overall range and in parenthesis the average of 12 measurements) are reported in the Table below:

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Table 1

Width of inhibition zone			
Control	Confluent growth in all streaks on all plates		
	Minimum mm	Maximum mm	
5 Fibre with tolnaftate	0.2 (0.7)	2.6 (3.9)	

Human skin (provided by a chiropodist) was sterilised, ground into fine fragments and wetted with synthetic perspiration. It was then used as a culture medium for A. repens. A needle punched nonwoven fabric of open structure 10 was placed in a deep glass dish, to which was then added a known amount of the A. repens culture and fifty HDM. Sticky tape was affixed to the upper part of the dish wall to entrap HDM attempting to climb the wall. The dish was then cultured for eight weeks at room temperature and 75% R.H. 15 The number of HDM stuck to the tape was recorded. Live HDM associated with the fabric were driven out by application of heat, and their number was recorded. The results shown in Table 2 were obtained (average of three cultures in each case).

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Table 2

Fabric	HDM on tape	HDM with fabric	Total
Amicor AF	36.6	16.0	42.6
Amicor AB	21.7	1.3	23.0
50/50 Amicor AF/Amicor AB	11.3	2.3	13.6
25 Courtelle	32.3	46.0	78.3

AMICOR AB (Trade Mark of Courtaulds Fibres (Holdings) Limited) is an acrylic fibre containing triclosan made in similar manner to AMICOR AF.

The average number of HDM associated with the Amicor AF 30 fabric may be distorted by an apparent rogue result; the individual numbers recorded were 4, 9 and 35.

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If a large number of HDM is found associated with the fabric, the presence of HDM on the tape suggests a thriving culture which is attempting to colonise other areas. If a small number of HDM is found associated with the fabric, the presence of HDM on the tape suggests an attempt by HDM to emigrate from a barren environment.

In comparative experiments, the same procedure was followed except that a synthetic food medium for HDM was used instead of the A. repens culture. HDM thrived on all the samples, 10 and there was no significant difference in HDM numbers between any of the samples.

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CLAIMS

1. The use of a polymeric article having incorporated therein a chemical compound which has antifungal activity against fungi of the groups Aspergillus glaucus and/or A. restrictus as a means of controlling house dust mites and bedmites.

2. The use according to claim 1, wherein the polymeric article is a fibre.

3. The use according to claim 2, wherein the fibre is 10 a manmade fibre into which the chemical compound was incorporated during the course of its manufacture.

4. The use according to claim 3, wherein the fibre is an acrylic fibre.

5. The use according to any one of claims 2 to 4, 15 wherein the fibre is incorporated in a textile article.

6. The use according to claim 5, wherein the textile article is a bedding fabric.

7. The use according to claim 1, wherein the polymeric article is a foam.

20 8. A filling material for an article of bedding or an upholstered article, characterised in that in said filling material is incorporated a compound which exhibits antifungal activity against fungi of the groups Aspergillus glaucus and/or A. restrictus.

25 9. An article of bedding or upholstered article, characterised in that it is filled with a filling material according to claim 8.

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10. A bedding fabric, characterised in that it comprises fibre having incorporated therein a chemical compound which has antifungal activity against fungi of the groups Aspergillus glaucus and/or A. restrictus.

ABSTRACT

METHODS OF CONTROLLING HOUSE DUST MITES AND BEDMITES

Polymeric articles such as fibres and foams having incorporated therein a chemical compound which has 5 antifungal activity against fungi of the groups Aspergillus glaucus and/or A. restrictus are useful in controlling house dust mites and bedmites (Dermatophagooides spp.).

Attorney's Cockett No. _____

COMBINED DECLARATION AND POWER OF ATTORNEY

(ORIGINAL, DESIGN, NATIONAL STAGE OF PCT, SUPPLEMENTAL, DIVISIONAL,
CONTINUATION OR CIP)

As a below named inventor, I hereby declare that:

TYPE OF DECLARATION

This declaration is of the following type: (check one applicable item below)

original
 design
 supplemental

NOTE: If the declaration is for an international Application being filed as a divisional continuation or continuation-in-part application do not check next item; check appropriate one or last three items.

national stage of PCT

NOTE: If one of the following 3 items apply then complete and also attach ADDITIONAL PAGES FOR DIVISIONAL
CONTINUATION OR CIP

divisional
 continuation
 continuation-in-part (CIP)

INVENTORSHIP IDENTIFICATION

WARNING: If the inventors are each not the inventors of all the claims an explanation of the facts, including the ownership of all the claims at the time the last claimed invention was made, should be submitted.

My residence, post office address and citizenship are as stated below next to my name. I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

TITLE OF INVENTION

METHODS OF CONTROLLING HOUSE DUST MITES AND BED MITES

SPECIFICATION IDENTIFICATION

the specification of which: (complete (a), (b) or (c))

(a) is attached hereto.
(b) was filed on _____ as Serial No. 0 / _____
or Express Mail No., as Serial No. not yet known _____
and was amended on _____ (if applicable).

NOTE: Amendments filed after the original papers are deposited with the PTO which contain new matter are not accorded a filing date by being referred to in the declaration. Accordingly, the amendments involved are those filed with the application papers or, in the case of a supplemental declaration, are those amendments claiming matter not encompassed in the original statement of invention or claims. See 37 CFR 1.57.

(Declaration and Power of Attorney [1-1]—page 1 of 4)

(c) was described and claimed in PCT International Application No. PCT/GB98/03137 filed on 21 October 1998 and as amended under PCT Article 19 on _____ (if any).

ACKNOWLEDGEMENT OF REVIEW OF PAPERS AND DUTY OF CANDOR

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, § 1.56(a).

In compliance with this duty there is attached an information disclosure statement, 37 CFR 1.97.

PRIORITY CLAIM

I hereby claim foreign priority benefits under Title 35, United States Code, § 119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed.

(complete (d) or (e))

(d) no such applications have been filed.
(e) such applications have been filed as follows.

NOTE. Where item (c) is entered above and the International Application which designated the U.S. claimed priority check item (e), enter the details below and make the priority claim

EARLIEST FOREIGN APPLICATION(S), IF ANY FILED WITHIN 12 MONTHS (6 MONTHS FOR DESIGN) PRIOR TO THIS U.S. APPLICATION

COUNTRY	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED UNDER 37 USC 119
GB	9722448.9	23.10.97.	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
			<input type="checkbox"/> YES <input type="checkbox"/> NO
			<input type="checkbox"/> YES <input type="checkbox"/> NO
			<input type="checkbox"/> YES <input type="checkbox"/> NO
			<input type="checkbox"/> YES <input type="checkbox"/> NO

ALL FOREIGN APPLICATION(S), IF ANY FILED MORE THAN 12 MONTHS (6 MONTHS FOR DESIGN) PRIOR TO THIS U.S. APPLICATION

POWER OF ATTORNEY

As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. (List name and registration number)

Stanley B. KITA, Registration No. 24,561; George A. SMITH, Jr., Registration No. 24,442; Wilson OBERDORFER, Registration No. 17,379; Mary E. BAK, Registration No. 31,215; Henry HANSEN, Registration No. 19,612 and Cathy Ann KODROFF, Registration No. 33,980

Attached as part of this declaration and power of attorney is the authorization of the above-named attorney(s) to accept and follow instructions from my representative(s)

SEND CORRESPONDENCE TO

DIRECT TELEPHONE CALLS TO:
(Name and telephone number)

HOWSON AND HOWSON
Spring House Corporate Center,
P.O. Box 457, Spring House,
Pennsylvania 19477.

(215) 540-9200

DECLARATION

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

SIGNATURE(S)

RC Full name of sole or first inventor Roland COX
Inventor's signature R. Cox
Date 10th April 2000 Country of Citizenship United Kingdom
Residence Derby, United Kingdom
Post Office Address 11 Wickersley Close, Darley Abbey, DE22 2XT
United Kingdom GBX

Full name of second joint inventor, if any _____
Inventor's signature _____
Date _____ Country of Citizenship _____
Residence _____
Post Office Address _____

CHECK PROPER BOX(ES) FOR ANY OF THE FOLLOWING ADDED PAGE(S) WHICH
FORM A PART OF THIS DECLARATION

Signature for third and subsequent joint inventors. *Number of pages added* _____

Signature by administrator(trix), executor(trix) or legal representative for deceased or incapacitated inventor. *Number of pages added* _____

Signature for inventor who refuses to sign or cannot be reached by person authorized under 37 CFR 1.47. *Number of pages added* _____

* * *

Added pages to combined declaration and power of attorney for divisional, continuation, or continuation-in-part (CIP) application.

Number of pages added _____

* * *

Authorization of attorney(s) to accept and follow instructions from representative

If no further pages form a part of this Declaration then end this Declaration with this page and check the following item

This declaration ends with this page

ADDED PAGE TO COMBINED DECLARATION AND POWER OF ATTORNEY
FOR AUTHORIZATION OF ATTORNEY(S) TO ACCEPT AND FOLLOW
INSTRUCTIONS FROM REPRESENTATIVE

The undersigned to this declaration and power of attorney hereby authorizes the U.S. attorney(s) named herein to accept and follow instructions from

JY & GW Johnson

Name(s) of authorized representative(s)

Kingsbourne House,

Address

229-231 High Holborn,

London WC1V 7DP ENGLAND

as to any actions to be taken in the Patent and Trademark Office regarding this application without direct communication between the U.S. attorney(s) and the undersigned. In the event of a change in the person(s) from whom instructions may be taken, the U.S. attorney(s) will be so notified by the undersigned.

(Added page to Combined Declaration and Power of Attorney for authorization of attorney(s) to accept and follow instructions from representative [1-24])